Osteoporosis Definition:

A systemic disease characterized by low bone mass and micro-architectural deterioration of the skeleton, leading to enhanced bone fragility and increased risk of fracture.

Why Care About Osteoporosis?

- In the U.S., 10 million with osteoporosis and 34 million with osteopenia
- Causes ~2 million fractures/yr
- After age 65, 1 in 2 women and 1 in 5 men will sustain an osteoporotic fracture
- Results in ~2.5 million physician visits, >400,000 hospital admits, and >180,000 NH admits = $25 billion by 2025 in direct costs

Learning Objectives

- Define the morbidity associated with osteoporosis
- Diagnose osteoporosis by clinical criteria and DXA t-scores
- Recommend appropriate prevention and treatment of osteoporosis

Osteoporosis Risk Factors

- Female sex
- White/Asian ancestry
- Early Menopause
- Increasing Age/Postmenopausal
- Fracture in 1st degree relative
- Genetic disorders
- Nulliparity
- Low Body Weight
- Excessive caffeine
- Sedentary lifestyle
- Drugs

Why Care About Osteoporosis?

- In U.S., the majority of patients with fragility fractures do not receive osteoporosis therapy
- In one study of women >65yo with recent hip fracture, 13% were receiving adequate treatment for osteoporosis
Prevalence of Osteoporosis Increases with Age

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>5%</td>
</tr>
<tr>
<td>70</td>
<td>50%</td>
</tr>
<tr>
<td>80</td>
<td>75%</td>
</tr>
</tbody>
</table>

Average age at time of hip fracture is 75

Following a Hip Fracture, Remember the “Rule of 4th’s”
- Dead
- Institutionalized
- Alive, no change in function
- Home with new functional deficits

**80% of women >75 yrs old would prefer death to a hip fracture resulting in nursing home admit**

Osteoporosis – May Be Silent!
- Pain may be minimal with fracture
- Loss of height
- Kyphosis

Osteoporosis – WHO Definition

<table>
<thead>
<tr>
<th>T Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; -1 SD</td>
<td>Normal</td>
</tr>
<tr>
<td>-1 to -2.5 SD</td>
<td>Low bone mass (Osteopenia)</td>
</tr>
<tr>
<td>&lt; - 2.5 SD</td>
<td>Osteoporosis</td>
</tr>
<tr>
<td>&lt; - 2.5 SD plus one or more fractures</td>
<td>Severe or established osteoporosis</td>
</tr>
</tbody>
</table>

The Z-score
- A measure of age and sex matched BMD
- A Z-score of < -2.0 may indicate a secondary cause of bone loss
- The Z-scores are used for diagnosis of osteoporosis in children, younger women and men < 50 yo

Bone Mineral Density Test DXA (Dual Energy X-ray Absorptiometry)
- The WHO criteria for osteoporosis are based on DXA
- Hip DXA is the best predictor of hip fracture which is the most clinically relevant site of fracture
How DXA (Dual-energy X-ray Absorptiometry) Works

- X-ray tube generates photon beams of 2 energy levels ("dual energy")
- Difference in attenuation of two beams as they pass thru tissue distinguishes bone from soft tissue; denser, thicker tissue (bone) contains more electrons and allows fewer photons to pass thru detector
- Proprietary software interprets results

Ultrasound

- Ultrasonic measurement of heel bone density predicts fracture risk and costs less per exam
- Correlation with DXA is poor, even though both predict fracture risk
- DXA is considered the "gold standard"

Who Needs BMD Testing?

<table>
<thead>
<tr>
<th>Patient category</th>
<th>USPSTF</th>
<th>NOF</th>
<th>ISCD</th>
</tr>
</thead>
<tbody>
<tr>
<td>All women age ≥ 65 years</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>All men aged ≥ 70 years</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Men and women 50-69 based on the risk factors</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>All women 60-64 based on the risk factors</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Who Needs BMD Testing?

<table>
<thead>
<tr>
<th>Patient category</th>
<th>USPSTF</th>
<th>NOF</th>
<th>ISCD</th>
</tr>
</thead>
<tbody>
<tr>
<td>All men and women with a fragility fracture</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Anyone considering treatment for osteoporosis</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Anyone receiving treatment for osteoporosis</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

WHO Fracture Risk Assessment FRAX!

- Combines above risk factors with hip BMD
- Calculates 10 year probability of hip fracture and 10 year probability of any major osteoporotic fracture

WHO FRAX Risk Assessment

- Web-based Tool
- Current smoking
- Glucocorticoid use
- Rheumatoid arthritis
- Secondary osteoporosis
- Alcohol > 3 drinks/day
- Combines above risk factors with hip BMD
- Calculates 10 year probability of hip fracture and 10 year probability of any major osteoporotic fracture

http://www.sheffield.ac.uk/FRAX/
All Patients Need Work-up to Rule out Secondary Osteoporosis

- CBC
- Chemistries
  - Renal function
  - Liver function
  - Ca, Phos
- Thyroid
- Testosterone (men)

25-Hydroxy vitamin D – 20%
24 hour urine calcium – 10%

Tannenbaum C et al. J clin Endocrinol Metab. 2002;87;4431

Osteoporosis

24-hour Urinary Calcium Excretion

<table>
<thead>
<tr>
<th>Elevated (&gt;250 mg/day)</th>
<th>Excessive calcium/vitamin D intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>High bone turnover states</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Low (&lt; 50 mg/day)</th>
<th>Idiopathic hypercalciuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malabsorption, e.g., Celiac disease</td>
<td></td>
</tr>
<tr>
<td>Calcium or Vitamin D deficiency</td>
<td></td>
</tr>
</tbody>
</table>

1. Which patient is least likely to have idiopathic osteoporosis?

A. Slender, 61-inch-tall, 71 yo Caucasian woman with a T12 vertebral fracture
B. 86 yo Caucasian man with a hip fracture
C. 65 yo thin, alcoholic Caucasian woman who smokes and has T10-T12 vertebral fx
D. 67 yo obese African-American woman with a T4 vertebral fracture

2. Which patient has a diagnosis of osteoporosis?

A. 74 yo woman incidentally noted to have a T12 compression fracture on a CXR ordered to evaluate for pneumonia
B. 65 yo man with a hip fracture after falling off a ladder
C. 88 yo man with lumbar spine T-score of -2.2
D. 79 yo woman with a T-score of -2.7 on heel ultrasound

Osteoporosis

- Short stature, slender, Caucasian women at greater risk for osteoporosis
- Risk of osteoporosis in men becomes similar to women in advanced age
- Alcohol and cigarette smoking accelerate this risk
- Osteoporotic fracture usually begins in vertebrae under greatest anatomical load (T12) and spread caudal and cephalad

© American Academy of Family Physicians. All Rights Reserved.
2. Which patient has a diagnosis of osteoporosis?

A. 74 yo woman incidentally noted to have a T12 compression fracture on a CXR ordered to evaluate for pneumonia

B. 65 yo man with a hip fracture after falling off a ladder

C. 88 yo man with lumbar spine T-score of -2.2

D. 79 yo woman with a T-score of -2.7 on heel ultrasound

Who Needs Treatment?

- Postmenopausal women and men > 50 yo
  - Hip or vertebral fracture
  - Prior fractures and low bone mass
  - T score ≤ -2.5 after appropriate evaluation for secondary causes
  - Low bone mass (T score -1 to -2.5) if high risk (e.g., glucocorticoid use)

OR

- 10 year probability > 3 % for hip fracture

OR

- 10 year probability of > 20% for any osteoporotic fracture (based on FRAX score)

3. Which woman has the highest risk for hip fracture?

A. 80 yo woman with a hip t-score -2.7

B. 65 yo woman with a hip t-score -2.7

C. 45 yo woman with a hip t-score -2.7

D. Hip fracture risk is the same for all 3

3. Which woman has the highest risk for hip fracture?

A. 80 yo woman with a hip t-score -2.7

B. 65 yo woman with a hip t-score -2.7

C. 45 yo woman with a hip t-score -2.7

D. Hip fracture risk is the same for all 3
Fracture Risk

• Fracture risk increase with age:
  – T score of -2.7 at age 80 = 7%/year
  – T score of -2.7 at age 65 = 3%/year
  – T score of -2.7 at age 45 = <1%/year

4. Which man has the highest risk for hip fracture?

A. 85 yo man with a hip t-score -2.7
B. 85 yo man with a hip t-score -2.7 and a prior vertebral fracture
C. Hip fracture risk is the same for both

Fracture Predicts Future Fracture

<table>
<thead>
<tr>
<th>Prior Fracture Site</th>
<th>Wrist</th>
<th>Vertebral</th>
<th>Hip</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist</td>
<td>3.3</td>
<td>1.7</td>
<td>1.9</td>
</tr>
<tr>
<td>Vertebral</td>
<td>1.4</td>
<td>4.4</td>
<td>2.3</td>
</tr>
<tr>
<td>Hip</td>
<td>N/a</td>
<td>2.5</td>
<td>2.3</td>
</tr>
</tbody>
</table>

5. Medicare will not pay for which patient’s DXA?

A. 72 yo woman who had a DXA 10 months ago, takes risedronate, and has a maternal history of hip fracture
B. 65 yo man with osteopenia noted on CXR
C. 78 yo woman with sarcoidosis on chronic prednisone therapy
D. 95 yo woman who takes no medications except HCTZ and has had no falls
Medicare Coverage for DXA

• Initial screening and then repeat screening no more frequently than every 24 months
• May repeat scan after 1 year to see if the treatment is working
• Whether repeated DXA measurements are cost-effective remains controversial

62-Year-Old Woman – Scans from the Same Day!

L1-L4 BMD = 1.247 g/cm²  T-Score = 0.6
L1-L4 BMD = 1.091 g/cm²  T-Score = 0.4

6. Which woman should get a DXA?
   A. 84 yo woman with falls, never had a DXA, on calcium and vitamin D, exercises regularly, willing to take a bisphosphonate
   B. 76 yo woman with PMR on chronic steroids, t-score of -2.3 on DXA 2 years ago; takes calcium and risedronate; not willing to consider PTH therapy (injections)
   C. 58 yo woman newly menopausal, BMI 32kg/m², sedentary, takes no medications or supplements, and has no family history of osteoporosis

Recommendations for Ordering a DXA

• “Utilizing any procedure to measure bone density is not indicated unless the results will influence the patient’s treatment decision.”

Osteoporosis Prevention & Treatment

• Everyone should be counseled about:
  – Weight-bearing exercise
  – Calcium and Vitamin D
  – Smoking cessation
  – Avoiding excessive alcohol intake
  – Fall prevention
• Consider hip protectors
7. Which of the following is the preferred daily dose of vitamin D and Calcium for postmenopausal women with osteoporosis?

A. 20mcg 25-hydroxyvitamin D + 600 mg calcium
B. 400 IU/day of Vitamin D3 + 1500 mg calcium
C. 800 IU/day of Vitamin D3 + 1200 mg calcium
D. 30 mcg 1,25-dihydroxyvitamin D + 1000 mg calcium
E. 800 IU/day of Vitamin D2 + 2000 mg calcium

Calcium

- Recommended intake is 1200 mg calcium/day for age 50+
- “Typical” woman in the U.S. gets about 600 mg from dietary sources
- 2500 mg/day is the maximum “safe” daily intake

Calcium Supplementation

- Most women need calcium supplementation
  - Calcium carbonate (cheap!)
    - Should be taken with a meal for optimal absorption.
  - Calcium citrate
    - May be taken without food
    - Preferred for patients with achlorhydria or long-term histamine H2 blockers or proton pump inhibitors

Vitamin D

- Vitamin D3 = cholecalciferol
- Vitamin D2 = ergocalciferol
- 25-hydroxyvitamin D3 = calcidiol
- 1,25-dihydroxyvitamin D3 = calcitriol

8. Which one of the following is the best test for vitamin D deficiency?

A. Serum ionized calcium
B. Serum 1,25 dihydroxyvitamin D level
C. Serum 25-hydroxyvitamin D level
D. 24-hour urine for calcium, alpha hydroxylase
8. Which one of the following is the best test for vitamin D deficiency?

- A. Serum ionized calcium
- B. Serum 1,25 dihydroxyvitamin D level
- C. Serum 25-hydroxyvitamin D level
- D. 24-hour urine for calcium, alpha hydroxylase

**Correct Answer:** C. Serum 25-hydroxyvitamin D level

**Vitamin D Deficiency**
- <10ng/mL (25nmol/L)
- Found in >50% of medical inpatients and ~20% with hip fractures

**Vitamin D Insufficiency**
- <32 ng/mL (80 nmol/L)
- Found in ~75% of patients in a geriatric clinic

---

9. A 68 yo Caucasian woman with no other risk factors is worried about her risk for hip fracture. DXA is -1.5. She asks about taking medication to prevent a fracture.

- A. Prescribe low dose estrogen patch
- B. Prescribe alendronate
- C. Prescribe raloxifene
- D. None of the above

**Correct Answer:** D. None of the above

---

**Prevention of Osteoporosis**
- For the majority of post menopausal women, pharmacologic therapy (besides adequate calcium and vitamin D intake) is not recommended
- For post menopausal women with one or more risk factors but DXA >-2.5, treatment may be offered (dose of alendronate is half of treatment dose, i.e., 35 mg weekly)

**Treatment of Osteoporosis**
- Bisphosphonates oral (alendronate, risedronate, ibandronate) or IV (zoledronic acid)
- Raloxifene
- Calcitonin
- Estrogen/androgens
- PTH
- Denosumab
10. Which of the following has been shown to reduce the risk of hip fracture?

- A. Raloxifene
- B. Alendronate
- C. Ibandronate
- D. Calcitonin

**FDA-Approved Treatment**

<table>
<thead>
<tr>
<th>Antiresorptive (bone retaining)</th>
<th>Postmenopausal osteoporosis</th>
<th>Men</th>
<th>Gluocorticoid induced osteoporosis (GIOP)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medication</strong></td>
<td><strong>+ + +</strong></td>
<td><strong>+ + +</strong></td>
<td><strong>+ + +</strong></td>
</tr>
<tr>
<td>Alendronate</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Risedronate</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Zoledronate</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Ibandronate</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Raloxifene</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Calcitonin</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* GIOP – Glucocorticoid induced osteoporosis

**Bisphosphonates**

- Given on an empty stomach with full glass of water
- Contraindications
  - Esophageal stricture
  - Achalasia
  - Patients who are unable to stand or sit upright
  - Renal failure with creatinine clearance of < 35 mL/minute
  - Hypocalcemia

**Bisphosphonates – Osteonecrosis of Jaw**

- Low incidence
- Most often with IV bisphosphonates
- Mostly in cancer patients
- Maintain oral hygiene
- Regular dental check-up

**Bisphosphonates – Long-Term Use Linked to Atypical Fractures**

- Low-energy subtrochanteric femoral and pelvic insufficiency fractures
- Poor healing
- Consider stopping bisphosphonate after 5-10 years

*J Clin Endocrinol Metab* April, 2010, 95(4)
Raloxifene

- Formerly Selective Estrogen Receptor Modulator ("SERM")
- Estrogen agonist/antagonist
- Reduces risk of breast cancer
- Does not stimulate endometrium
- Hot flashes
- Has not been shown to reduce hip fracture risk; less potent than bisphosphonates

11. Which osteoporosis therapy has an analgesic effect in the setting of acute vertebral fracture?

A. Alendronate
B. Calcitonin
C. Estrogen
D. Teriparatide

Calcitonin

- Calcitonin – Polypeptide hormone
  - Most useful in vertebral fracture complicated by pain for analgesic benefit
  - Weak antifracture efficacy
  - Remember to prescribe calcium and vitamin D!

12. Which statement about PTH therapy for osteoporosis is correct?

A. Improves BMD but does not decrease fracture risk
B. Treatment of choice for Paget’s disease
C. After 5 years of PTH therapy, BMD remains stable for the next 2 years
D. The most common side effects of PTH are nausea, dizziness, and leg cramps
Teriparatide (PTH) Parathyroid Hormone (1-34)

- Daily SQ injections
- Reserved for pts with high risk for fractures
  - Multiple fractures
  - Extremely low BMD e.g. < -3
  - Intolerant/unresponsive to other Rx
- FDA black box warning: osteosarcoma (animals), thus, safety and efficacy > 2 yrs
- Consider adding bisphosphonate after 2 yrs

Denosumab (Prolia)

- Monoclonal antibody against RANKL (receptor that stimulates osteoclastic activity)
- Reduces vertebral, hip and nonvertebral fractures
- No long-term safety data
- Role is controversial
- Expensive

Follow-up of Patients on Treatment

- DXA; some argue no reason to repeat
- Bone loss while on treatment
  - Is Ca and vitamin D intake adequate?
  - Is the patient taking medications as prescribed?
  - Is something else causing bone loss?

13. Do hip protectors prevent hip fractures?

A. Yes
B. No
C. Maybe
D. All of the above

36% Yes
24% No
33% Maybe
7% All of the above

Hip Protectors

Hip Protectors

• Initial studies suggested hip fracture benefits for nursing home residents (NNT @ 24)
• Studies in community dwelling adults suggested benefits for compliant subjects
• Recent study in nursing home residents raises questions about efficacy: using a one-sided hip protector, no difference in fracture rates between sides
  – (DP Kiel et al, JAMA, 2007; 298:413-22)

Answers

1. D
2. A
3. A
4. B
5. A
6. A
7. C
8. C
9. D
10. B
11. B
12. D
13. ??